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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/090,672	06/04/98	ISHIWATA	T 766.21

005514
FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK NY 10112

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EXAMINER	
BRUNOVSKIS,P	
ART UNIT	**PAPER NUMBER**
1632	20

DATE MAILED: 06/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/090,672	Ishiwata et al.
Examiner	**Art Unit**
Peter Brunovskis	1632

-- Th MAILING DATE of this communication appears on th cover she t with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 4/09/01 and 5/03/01

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1, 2, 4-7, 18, and 19 is/are pending in the applica

4a) Of the above, claim(s) 6 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1, 2, 4, 5, 7, 18, and 19 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☒ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

The request filed on 5/03/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/090,672 is acceptable and a CPA has been established. An action on the CPA follows.

Applicant's arguments and amendments filed 4/09/01 and 5/03/01 have been entered and will only be considered or addressed to the extent that they apply to the claims under examination. Unless otherwise indicated, arguments directed to rejections or objections rendered moot in view of Applicants amendments will not be further acknowledged or addressed.

Election/Restriction

Claim 6 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made with traverse in the Interview Summary attachment to Paper No. 8. However, the election has been treated as an election without traverse, since applicant did not distinctly and specifically point out the supposed errors in the restriction requirement (MPEP § 818.03(a)).

The status of claim 6 remains unclear as set forth in the Office Action of 12/05/00. Although claim 6 is drawn to a non-elected invention as set forth in Paper No. 8 filed 2/15/00, the response filed 8/28/00 (Paper No. 13) states: "By the above *cancellation* of claims 6, 8, 9, 14-17,

20 and 21 the provisional Election is hereby affirmed" (sentence abridging p. 4-5; emphasis added). However, elsewhere the response instructs to "Please cancel Claims 3, 8-17, 20 and 21" (top of p. 2) and additionally states that "Claims 1, 2, 4-7, 18 and 19 remain presented for continued prosecution" (middle of p. 8). Neither the after-final response of 4/09/01, nor the response 5/03/01 have addressed this discrepancy. Clarification is requested.

Claim Objections

Claim 1 is objected to because of the following informalities: In claim 1, "immobolized" is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, 2, 4, 5, 7, 18, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and dependent claims) is indefinite in its recitation of the phrase "a DNA which hybridizes with said DNA...followed by washing the filter..." since it is unclear what temporal relationship exists between the washing step and the hybridization step or whether the DNA is

hybridizing to itself or some other DNA. For example, it is not clear whether the DNA hybridizes to a filter that has been washed, whether the DNA hybridizes to filter and then washed or whether the DNA hybridizes in such a way as to maintain stable association with the recited in the presence of the wash step.

Claim 1 (and dependent claims) recites the limitation "said DNA" in line 6. There is insufficient antecedent basis for this limitation in the claim. The claim recites "an isolated DNA" in line 1 and "a DNA" in line 6.

Claim 2 (and dependent claims) is indefinite in its recitation of the phrase "the open reading frames of SEQ ID NOs:1-6", since it is unclear which specific open reading frames the phrase is directed to.

Claim 4 is an incomplete claim since the method fails to recite any method steps that relate back to the preamble drawn to a method of detecting mRNA. Furthermore, the claim is indefinite because it is unclear whether the method is directed to detection of any specific mRNA or whether the method is broadly directed to a generic method of mRNA detection, independent of the source or type. The response of 4/09/01 argues that "the recited mRNA is restricted to only those mRNA that can be detected by the DNA of claims 1 or 2 rather than to any random mRNA". However, this argument does not overcome the previous grounds for indefiniteness since it relies on features that are not in the instant claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4, 5, 7, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 2, 4, 5, 7, 18, and 19 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. Applicant is reminded of the factors for determining enablement as set forth in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988) factors for evaluating undue experimentation include the amount of direction or guidance presented.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly

conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure*" (emphasis added).

Although the specification provides support for isolated DNAs comprising a nucleotide sequence identical to contiguous 10 to 50 residues selected from the nucleotide sequences represented by SEQ ID NOs:1-6 (and 9-12) in accordance with the teachings from the specification (e.g. p. 8, lines 1-4), the specification does not provide support for such embodiments being limited to the open reading frames of SEQ ID NOs:1-6, nor for the use of such embodiments as diagnostic or therapeutic agents. There is no evidence that Applicants envisioned or were in possession of the broad genera of products and methods of using such at the time of filing.

Claims 1, 2, 4, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using isolated DNAs comprising the nucleotide sequences of SEQ ID NOs:1-6 and 9-12, does not reasonably provide enablement for the full

scope of isolated DNAs hybridizing with said SEQ ID NOs or comprising a nucleotide sequence identical to any continuous 10 to 50 residues therefrom. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed invention is broadly drawn to compositions and methods comprising the use of isolated DNAs comprising the nucleotide sequences of SEQ ID NOs:1-6 and 9-12; isolated DNAs hybridizing to such, and isolated DNA comprising a nucleotide sequence identical to any continuous 10-50 residues therefrom. Because the claimed embodiments are embraced by nucleic acid embodiments disclosed in the prior art from unrelated organisms or with no connection to IgA nephropathy, particularly since any given 100-1000 base pair sequence would be expected to contain multiple matches to unrelated nucleotide sequences containing at least 10 continuous residues, as evidenced by unrelated prior art disclosures revealing matches of at least 17 nucleotides to any of the given 10 SEQ ID NOs examined in the instant application (see below). The specification does not teach how to use nucleic acids lacking the ability to discriminate between products exemplified by SEQ ID NOs 1-6 and 9-12 that are upregulated in IgA nephropathy and unrelated products comprising matches of only 10 continuous residues of SEQ ID NOs 1-6 or comprising sequences capable of hybridizing to SEQ ID NOs 1-6 and 9-12, given the fairly low stringency conditions recited in claim 1. The specification does not provide a basis or a methodology for predicting *a priori*, absent undue experimentation, those embodiments

embraced by the scope of the claims that have a patentable utility in e.g. diagnostics (or other), in accordance with the teachings in the specification.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 is drawn to a method of treating IgA nephropathy comprising administration of a composition comprising the DNA of claim 2 "to a patient in need thereof". The specification provides no guidance for using the claimed invention for treating IgA nephropathy. Importantly, the specification provides no evidence for a cause-effect relationship between the upregulated genes detected from patients with IgA nephropathy and the disease. In the absence of such information validating the premise of treatment or of any working examples or evidence linking downregulation of the genes exemplified by SEQ ID NOs:1-6 and 9-12 to a therapeutic effect, there would be no expectation of success and an undue level of experimentation at the very least, particularly in view of the lack of guidance concerning the design and *in* vivo targeting of therapeutic oligonucleotide agents against IgA nephropathies and the above problems with respect to spurious binding.

The instant invention, as claimed, falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may not be workable". The

court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genentech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005). The methods of treatment in the claimed invention constitute such a "germ of an idea".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The Table below sets forth prior art that applies to the SEQ ID NOs. elected for examination and includes the positions of identity between the claimed sequence and that of the prior art.

SEQ ID NO	Reference	Location in Reference	Location in claimed SEQ ID NO	Location in Prior art SEQ
1	Hillier et al. (10/26/95)	GenBank Accession No. H71225	189-536	51-398
2	Bader et al. (5/16/96)	GenBank Accession No. U23946	38-518	1-481
3	Hettmann et al. (9/23/94)	GenBank Accession No. S71037	1352-1371	117-136
4	Kelly et al. (4/24/93)	GenBank Accession No. X02228	650-667	14483-14500

5	Kelly et al. (4/24/93)	GenBank Accession No. X02228	1005-1022	14483-14500
6	Hillier et al. (4/02/96)	GenBank Accession No. N89899	95-528	1-435*
9	Hillier et al. (10/31/95)	GenBank Accession No. H73595	32-48	304-320*
10	Trick (3/23/95)	GenBank Accession No. X52089	92-109	1879-1896
11	Hudson (5/31/96)	GenBank Accession No. G24450	52-69	258-275
12	Hillier et al. (3/31/95)	GenBank Accession No. T98890	31-251	2-224

*complementary sequence of SEQ ID subsequence

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hillier et al. (GenBank Accession Number H71225, 10/26/95). Hillier et al. disclose a polynucleotide comprising 348 contiguous residues (nucleotides 51-398) identical to nucleotides 189-536 of SEQ ID NO:1, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bader et al. (GenBank Accession Number U23946, 5/16/96). Bader et al. disclose a polynucleotide comprising a segment (nucleotides 1-481) 99.6% identical to nucleotides 38-518 of SEQ ID NO:2, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Hettmann et al. (GenBank Accession Number S71037, 9/23/94). Hettmann et al. disclose a polynucleotide comprising a segment (nucleotides 117-136) identical to nucleotides 1352-1371 of SEQ ID NO:3, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelly et al. (GenBank Accession Number X02228, 4/24/93). Kelly et al. disclose a polynucleotide comprising a segment (nucleotides 14483-14500) identical to nucleotides 650-667 of SEQ ID NO:4 and nucleotides 1005-1022 of SEQ ID NO:5, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hillier et al. (GenBank Accession Number N89899, 4/02/96). Hillier et al. disclose a polynucleotide comprising a segment (nucleotides 1-435), whose complement is 99.8% identical to nucleotides 95-528 of SEQ ID NO:6, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank Accession Number H73595, 10/31/95). Hillier et al. disclose a polynucleotide

comprising a segment (nucleotides 304-320), whose complement is identical to nucleotides 32-48 of SEQ ID NO:9, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Trick (GenBank Accession Number X52089, 3/23/95). Trick discloses a polynucleotide comprising a segment (nucleotides 1879-1896) identical to nucleotides 92-109 of SEQ ID NO:10, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Hudson (GenBank Accession Number G24450, 5/31/96). Hudson discloses a polynucleotide comprising a segment (nucleotides 258-275) identical to nucleotides 52-69 of SEQ ID NO:11, to which it would hybridize given the recited hybridization conditions.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank Accession Number T98890, 3/31/95). Hillier et al. disclose a polynucleotide comprising a segment (nucleotides 2-224) identical to nucleotides 31-251 of SEQ ID NO:12, to which it would hybridize given the recited hybridization conditions.

Claims 18 and 19 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hillier et al. (GenBank Accession Number

H71225, 10/26/95), Bader et al. (GenBank Accession Number U23946, 5/16/96), Hettmann et al. (GenBank Accession Number S71037, 9/23/94), Kelly et al. (GenBank Accession Number X02228, 4/24/93), Hillier et al. (GenBank Accession Number N89899, 4/02/96), Hillier et al. (GenBank Accession Number H73595, 10/31/95), Trick (GenBank Accession Number X52089, 3/23/95), Hudson (GenBank Accession Number G24450, 5/31/96), Hillier (GenBank Accession Number T98890, 3/31/95).

GenBank Accession Numbers H71225, U23946, S71037, X02228, N89899, H73595, X52089, G24450, and T98890 have been described. None of the references explicitly recites the DNAs in conjunction with diagnostic- or pharmaceutical acceptable carriers. However, inasmuch as the DNA clones would have been implicitly resuspended in water or buffer, the references anticipate or make obvious the subject matter of claims 18 and 19.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

Peter Brunovskis, Ph.D.
Patent Examiner
Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER